Paper Alert

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A selection of interesting papers that were published in the month before our press date in major journals most likely to report significant results in structural biology, protein and RNA folding.

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Structure 1999, Vol 7 No 8:R191–R196

☐ Structural changes in the transition state of protein folding: alternative interpretations of curved chevron plots. Otzen DE, Kristensen O, Proctor M and Oliveberg M (1999). *Biochemistry **38**, 6499-6511*

The interpretation of folding rates is often rationalized within the context of transition state theory. Changes in the folding kinetics are thus caused by effects on either the ground state, the transition state, or both. However, structural changes of the transition state are rarely discussed in connection with experimental data, and kinetic anomalies are commonly ascribed to ground state effects alone. In this study, we present kinetic data which are best described by transition state changes. We also show that ground state effects and transition state effects are in general difficult to distinguish kinetically. The seemingly drastic effects of these mutations are readily ascribed to transition state movements where large kinetic differences result from relatively small alterations of a common free energy profile and broad activation barriers.
18 May 1999, *Biochemistry*

☐ Structure of a heterophilic adhesion complex between the human CD2 and CD58 (LFA-3) counterreceptors. Wang J, Smolyar A, Tan K, Liu J, Kim M, Sun Z, Wagner G and Reinherz EL (1999). *Cell* 97, 791-803.

Interaction between CD2 and its counterreceptor, CD58 (LFA-3), on opposing cells optimizes immune recognition, facilitating contacts between helper T lymphocytes and antigen-presenting cells as well as between cytolytic effectors and target cells. The authors report the crystal structure of the heterophilic adhesion complex between the amino-terminal domains of human CD2 and CD58. A strikingly asymmetric, orthogonal, face-to-face interaction involving the major β sheets of the respective immunoglobulin-like domains with poor shape complementarity is revealed. In the virtual absence of hydrophobic forces, interdigitating charged amino acid side chains form hydrogen bonds and salt links at the interface, imparting a high degree of specificity albeit with low affinity.
11 June 1999, *Cell*

☐ A structural explanation for the binding of multiple ligands by the α-adaptin appendage domain. Owen DJ, Vallis Y, Noble ME, Hunter JB, Dafforn TR, Evans PR and McMahon HT (1999). *Cell* 97, 805-815.

The α subunit of the endocytotic AP2 adaptor complex contains a 30 kDa 'appendage' domain, which is joined to the rest of the protein via a flexible linker. The 1.9 Å resolution crystal structure of this domain reveals a single binding site for its ligands, which include amphiphysin, Eps15, and epsin. This single site for binding multiple ligands would allow for temporal and spatial regulation in the recruitment of components of the endocytic machinery.
11 June 1999, *Cell*

☐ Structure of a voltage-dependent K^+ channel β subunit. Gulbis JM, Mann S and MacKinnon R (1999). *Cell* 97, 943-952.

The integral membrane subunits of many voltage-dependent potassium channels are associated with an additional protein known as the β subunit. One function of β subunits is to modify K^+ channel gating. The authors have determined the structure of the conserved core of mammalian β subunits by X-ray crystallography at 2.8 Å resolution. Like the integral membrane component of K^+ channels, β subunits form a four-fold symmetric structure. Each subunit is an oxido-reductase enzyme complete with a nicotinamide co-factor in its active site. Several structural features of the enzyme active site, including its location with respect to the four-fold axis, imply that it may interact directly or indirectly with the K^+ channel's voltage sensor.
25 June 1999, *Cell*

☐ Forced unfolding of fibronectin type 3 modules: an analysis by biased molecular dynamics simulations. Paci E and Karplus M (1999). *J. Mol. Biol.* 288, 441-459.

Titin, an important constituent of vertebrate muscles, is a protein of the order of a micrometer in length in the folded state. Atomic force microscopy and laser tweezer experiments have been used to stretch titin molecules to more than ten times their folded lengths. To explain the observed relation between force and extension, it has been suggested that the immunoglobulin and fibronectin domains unfold one at a time in an all-or-none fashion. We use molecular dynamics simulations to study the forced unfolding of two different fibronectin type 3 domains and of their heterodimer of known structure. An external biasing potential on the N to C distance is employed and the protein is treated in the polar hydrogen representation with an implicit solvation model. A series of simulations is performed for each system to obtain meaningful results. The two different fibronectin domains

are shown to unfold in the same way along two possible pathways. These involve the partial separation of the 'β-sandwich', an essential structural element, and the unfolding of the individual sheets in a stepwise fashion. For the two connected domains, there is complete unfolding of one domain (^{9}Fn3) before major unfolding of the second domain (^{10}Fn3). Comparison of different models for the potential energy function demonstrates that the dominant cohesive element in both proteins is due to the attractive van der Waals interactions; electrostatic interactions play a structural role but appear to make only a small contribution to the stabilization of the domains, in agreement with other studies of β-sheet stability.
7 May 1999, *Journal of Molecular Biology*

☐ **Rapid collapse and slow structural reorganisation during the refolding of bovine α-lactalbumin**. Forge V, Wijesinha RT, Balbach J, Brew K, Robinson CV, Redfield C and Dobson CM (1999). *J. Mol. Biol.* 288, 673-688

The refolding of bovine α-lactalbumin (BLA) from its chemically denatured state in 6 M GuHCl has been investigated by a variety of complementary biophysical approaches. CD experiments indicate that the species formed in the early stages of refolding of the *apo*-protein have at least 85% of the α-helical content of the native state, and kinetic NMR experiments show that they possess near-native compactness. Hydrogen exchange measurements using mass spectrometry and NMR indicate that persistent structure in these transient species is located predominantly in the α-domain of the native protein and is similar to that present in the partially folded A-state formed by the protein at low pH. There is no evidence for the existence of well-defined discrete kinetic intermediates of the type populated in the refolding of the structurally homologous c-type lysozymes. Rather, both mass spectrometric and NMR data indicate that the rate-determining transition from the compact partially structured (molten globule) species to the native state is highly cooperative. Taken together the results indicate that folding of BLA, in the presence of its four disulphide bonds, corresponds to one of the limiting cases of protein folding in which rapid collapse to a globule with a native-like fold is followed by a search for native-like side-chain contacts that enable efficient conversion to the close packed native structure.
14 May 1999, *Journal of Molecular Biology*

☐ **The structure of adrenodoxin reductase of mitochondrial *P* 450 systems: electron transfer for steroid biosynthesis**. Ziegler GA, Vonrhein C, Hanukoglu I and Schulz GE (1999). *J. Mol. Biol.* 289, 981-990.

Adrenodoxin reductase is a monomeric 51 kDa flavoenzyme that is involved in the biosynthesis of all steroid hormones. It receives a two-electron package from NADPH and converts it to two single electrons that are transferred *via* adrenodoxin to all mitochondrial cytochromes *P* 450. It shows neither sequence nor structural homology to established, functionally related electron transferases. Yet, the crystal structure reveals a relationship to the disulfide oxidoreductases, permitting the assignment of the NADP-binding site.
4 June 1999, *Journal of Molecular Biology*

☐ **Structure of aspartate-β-semialdehyde dehydrogenase from *Escherichia coli*, a key enzyme in the aspartate family of amino acid biosynthesis**. Hadfield A, Kryger G, Ouyang J, Petsko GA, Ringe D and Viola R (1999). *J. Mol. Biol.* 289, 991-1002.

Aspartate-β-semialdehyde dehydrogenase (ASADH) lies at the first branch point in an essential aspartic biosynthetic pathway found in bacteria, fungi and the higher plants. The crystal structure of the *Escherichia coli* enzyme shows that each monomer has an N-terminal nucleotide-binding domain and a dimerisation domain. The presence of an essential cysteine locates the active site in a cleft between the two domains. The functional dimer has the appearance of a butterfly, with the NADP-binding domains forming the wings and the dimerisation domain forming the body.
4 June 1999, *Journal of Molecular Biology*

☐ **Investigation of the interaction between DnaK and DnaJ by surface plasmon resonance spectroscopy**. Mayer MP, Laufen T, Paal K, McCarty JS and Bukau B (1999). *J. Mol. Biol.* 289, 1131-1144.

The interaction of the *E. coli* Hsp70 homologue, DnaK, with DnaJ was studied using surface plasmon resonance spectroscopy. Resonance signals of complex kinetic characteristics were detected when DnaK was passed over a sensor chip coupled with DnaJ. The interaction was specific. Detectable DnaK-DnaJ interaction required ATP hydrolysis by DnaK and was competitively inhibited by chaperone substrates of DnaK. Results suggest that DnaJ stimulates ATP hydrolysis only after association of a substrate with the substrate binding cavity of DnaK. This coupling mechanism required the J-domain of DnaJ, and was also functional for natural DnaK substrates, and thus is central to the mechanism of action of the DnaK chaperone system.
18 June 1999, *Journal of Molecular Biology*

☐ **The crystal structure of the human hepatitis B virus capsid**. Wynne SA, Crowther RA and Leslie AG (1999). *Mol. Cell* 3, 771-780.

Hepatitis B is a small enveloped DNA virus that poses a major hazard to human health. The crystal structure of the T = 4 capsid has been solved at 3.3 Å resolution, revealing a largely helical protein fold that is unusual for icosahedral viruses. The monomer fold is stabilized by a hydrophobic core that is highly conserved among human viral variants. Association of two amphipathic α-helical hairpins results in formation of a dimer with a four-helix bundle as the major central feature. The capsid is assembled from dimers via interactions involving a highly conserved region near the C terminus of the truncated protein used for crystallization. The major immunodominant region lies at the tips of the α-helical hairpins that form spikes on the capsid surface.
June 1999, *Molecular Cell*

☐ The crystal structure of rna1p: a new fold for a GTPase-activating protein. Hillig RC, Renault L, Vetter IR, Drell T IV, Wittinghofer A and Becker J (1999). *Mol. Cell* 3, 781-791.

rna1p is the Schizosaccharomyces pombe ortholog of the mammalian GTPase-activating protein (GAP) of Ran. Both proteins are essential for nuclear transport. Here, we report the crystal structure of rna1p at 2.66 Å resolution. It contains 11 leucine-rich repeats that adopt the nonglobular shape of a crescent, bearing no resemblance to RhoGAP or RasGAP. The invariant residues of RanGAP form a contiguous surface, strongly indicating the Ran-binding interface. Alanine mutations identify Arg-74 as a critical residue for GTP hydrolysis. In contrast to RasGAP and RhoGAP, Arg-74 could be substituted by lysine and contributed significantly to the binding of Ran. Therefore, we suggest a GAP mechanism for rna1p, which constitutes a variation of the arginine finger mechanism found for Ras GAP and RhoGAP.
June 1999, *Molecular Cell*

☐ Phosphatidylinositol 3-phosphate recognition by the FYVE domain. Kutateladze TG, Ogburn KD, Watson WT, de Beer T, Emr SD, Burd CG and Overduin M (1999). *Mol. Cell* 3, 805-811.

Recognition of phosphatidylinositol 3-phosphate (PtdIns(3)P) is crucial for a broad range of cellular signaling and membrane trafficking events regulated by phosphoinositide (PI) 3-kinases. PtdIns(3)P binding by the FYVE domain of human early endosome autoantigen 1 (EEA1), a protein implicated in endosome fusion, involves two β hairpins and an α helix. Specific amino acids, including those of the FYVE domain's conserved RRHHCRQCGNIF motif, contact soluble and micelle-embedded lipid and provide specificity for PtdIns(3)P over PtdIns(5)P and PtdIns, as shown by heteronuclear magnetic resonance spectroscopy. Although the FYVE domain relies on a zinc-binding motif reminiscent of RING fingers, it is distinguished by novel structural features and its PtdIns(3)P-binding site.
June 1999, *Molecular Cell*

☐ Structure and ligand of a histone acetyltransferase bromodomain. Dhalluin C, Carlson JE, Zeng L, He C, Aggarwal AK and Zhou M-M (1999). *Nature* 399, 491-496.

Histone acetylation is important in chromatin remodelling and gene activation. Nearly all known histone-acetyltransferase (HAT)-associated transcriptional co-activators contain bromodomains, which are ~110-amino-acid modules found in many chromatin-associated proteins. The solution structure of the bromodomain of the HAT co-activator P/CAF (p300/CBP-associated factor) reveals an unusual left-handed up-and-down four-helix bundle. Structural and site-directed mutagenesis studies show that bromodomains can interact specifically with acetylated lysine, making them the first known protein modules to do so.
3 June 1999, *Nature*

☐ Structural basis of procaspase-9 recruitment by the apoptotic protease-activating factor 1. Qin H, Srinivasula SM, Wu G, Fernandes-Alnemri T, Alnemri ES and Shi Y (1999). *Nature* 399, 549-557.

Caspase-9-mediated apoptosis (programmed cell death) plays a central role in the development and homeostasis of all multicellular organisms. Mature caspase-9 is derived from its procaspase precursor as a result of recruitment by the activating factor Apaf-1. The crystal structures of the caspase-recruitment domain of Apaf-1 by itself and in complex with the prodomain of procaspase-9 reveal that each molecule of Apaf-1 interacts with a molecule of procaspase-9 through two highly charged and complementary surfaces formed by non-conserved residues.
10 June 1999, *Nature*

☐ Basis for recognition of cisplatin-modified DNA by high-mobility-group proteins. Ohndorf U-M, Rould MA, He Q, Pabo CO and Lippard SJ (1999). *Nature* 399, 708-712.

The anticancer activity of cis-diamminedichloroplatinum(II) (cisplatin) arises from its ability to damage DNA, with the major adducts formed being intrastrand d(GpG) and d(ApG) crosslinks. These crosslinks bend and unwind the duplex, and the altered structure attracts high-mobility-group domain (HMG) and other proteins which may mediate the antitumour properties of the drug. Many HMG-domain proteins recognize altered DNA structures such as four-way junctions and cisplatin-modified DNA, but until now the molecular basis for this recognition was unknown. This paper describes mutagenesis, hydroxyl-radical footprinting and X-ray studies that elucidate the structure of a 1:1 cisplatin-modified DNA/HMG-domain complex.
17 June 1999, *Nature*

☐ The crystal structure of HasA, a hemophore secreted by ***Serratia marcescens***. Arnoux P, Haser R, Izadi N, Lecroisey A, Delepierre M, Wandersman C and Czjzek M (1999). *Nat. Struct. Biol.* 6, 516-520.

Free iron availability is strongly limited in vertebrate hosts, making the iron acquisition by siderophores inappropriate. Pathogenic bacteria have developed various ways to use the host's iron from iron-containing proteins. *Serratia marcescens* can use the iron from hemoglobin through the secretion of a hemophore called HasA, which takes up the heme from hemoglobin and shuttles it to the receptor HasR, which in turn releases heme into the bacterium. We report here the first crystal structure of such a hemophore, bound to a heme group at two different pH values and at a resolution of 1.9 Å. The structure reveals a new original fold and suggests a hypothetical mechanism for both heme uptake and release.
June 1999, *Nature Structural Biology*

☐ A novel two-chain proteinase inhibitor generated by previous acircularization of a multidomain precursor protein. Lee MC, Scanlon MJ, Craik DJ and Anderson MA (1999). *Nat. Struct. Biol.* 6, 526-530.

Female reproductive tissues of the ornamental tobacco amass high levels of serine proteinase inhibitors (PIs) for protection against pests and pathogens. These PIs are produced from a precursor protein composed of six repeats each with a protease reactive site. Here we show that proteolytic processing of the precursor generates five single-chain PIs and a remarkable two-chain inhibitor formed by disulfide-bond linkage of N- and C-terminal peptide fragments. Surprisingly, PI precursors adopt this circular structure regardless of the number of inhibitor domains, suggesting this bracelet-like conformation is characteristic of the widespread potato inhibitor II (Pot II) protein family.
June 1999, *Nature Structural Biology*

☐ Chain collapse can occur concomitantly with the rate-limiting step in protein folding. Plaxco KW, Millett IS, Segel DJ, Doniach S and Baker D (1999). *Nat. Struct. Biol.* 6, 554-556.

Time-resolved, small-angle X-ray scattering is used to characterise the extent of chain collapse early in the folding of protein L. Immediately after initiation of folding the protein has dimensions indistinguishable from those of the fully unfolded protein measured in high concentrations of denaturant under equilibrium conditions. This expanded state collapses to a more compact state with the same kinetics as the folding reaction. Thus, chain compaction does not need to precede the rate-limiting step in folding and rapid chain collapse is not an obligatory feature of protein folding reactions.
6 June 1999, *Nature Structural Biology*

☐ Acceleration of the refolding of Arc repressor by nucleic acids and other polyanions. Rentzeperis D, Jonsson T and Sauer RT (1999). *Nat. Struct. Biol.* 6, 569-573.

The refolding of the Arc repressor dimer can be accelerated 30-fold by negatively charged polymers including single-stranded and double-stranded DNA, RNA, and polyvinylsulphate but not by neutral or positively charged polymers. The salt-dependence of the polyanion-mediated process, as well as mutant studies, indicate that electrostatic interactions are important in this rate enhancement. Urea-dependence studies suggest that the Arc repressor is largely unstructured in the transition state for polyanion-mediated folding. At low ionic strength the observed kinetics are consistent with a model in which denatured monomers bind rapidly and nonspecifically to the polyanion and complete folding in the bound state.
6 June 1999, *Nature Structural Biology*

☐ Structure, specificity and CDR mobility of a class II restricted single-chain T-cell receptor. Hare BJ, Wyss DF, Osburne MS, Kern PS, Reinherz EL and Wagner G (1999). *Nat. Struct. Biol.* 6, 574-581.

Using NMR spectroscopy, the authors determined the solution structure of a single-chain T-cell receptor (scTCR) derived from the major histocompatibility complex (MHC) class II-restricted D10 TCR. The conformations of complementarity-determining regions (CDRs) 3β and 1α and surface properties of 2α are different from those of related class I-restricted TCRs. We infer a conserved orientation for TCR V(α) domains in complexes with both class I and II MHC-peptide ligands, which implies that small structural variations in Vα confer MHC class preference. High mobility of CDR3 residues relative to other CDR or framework residues (picosecond time scale) provides insight into immune recognition and selection mechanisms.
June 1999, *Nature Structural Biology*

☐ **The formation of a native-like structure containing eight conserved hydrophobic residues is rate-limiting in two-state folding of ACBP.** Kragelund BB, Osmark P, Neergaard TB, Schiodt J, Kristiansen K, Knudsen J and Poulsen FM (1999). *Nat. Struct. Biol.* 6, 594-601.

Protein engineering techniques and ϕ-value analysis are combined to characterise the structure of the transition state for folding of ACBP. The stability and kinetics of folding and unfolding of wild-type and 24 mutant proteins were measured. Eight residues were determined to have high ϕ-values, indicating that the side chains of these residues make a significant number of interactions in the transition state. Thus, these residues are important in stabilising the transition state and in ensuring rapid folding. These eight residues are hydrophobic and are located on the interface between N- and C-terminal helices. A sequential framework model is proposed.
6 June 1999, *Nature Structural Biology*

☐ Asymmetric DNA bending in the Cre-loxP site-specific recombination synapse. Guo F, Gopaul DN and Van Duyne GD (1999). *Proc. Natl Acad. Sci. USA* 96, 7143-7148

Cre recombinase catalyzes site-specific recombination between two 34-bp loxP sites in a variety of DNA substrates. At the start of the recombination pathway, the loxP sites are each bound by two recombinase molecules, and synapsis of the sites is mediated by Cre-Cre interactions. The authors describe the structures of synaptic complexes formed between a symmetrized loxP site and two Cre mutants that are defective in strand cleavage. The DNA in these complexes is bent sharply at a single base pair step at one end of the crossover region in a manner that is atypical of protein-induced DNA bends. The bend direction of the site appears to determine which of the two DNA substrate strands will be cleaved and exchanged in the initial stages of the recombination pathway.
22 June 1999, *Proceedings of the National Academy of Science USA*

☐ mRNA cap recognition: dominant role of enhanced stacking interactions between methylated bases and protein aromatic side chains. Hu G, Gershon PD, Hodel AE and Quiocho FA (1999). *Proc. Natl Acad. Sci. USA* 96, 7149-7154.

The authors have determined, by X-ray analysis, ten structures comprising the mRNA cap-specific methyltransferase VP39 or specific mutants thereof in the presence of methylated nucleobase analogs (N1-methyladenine, N3-methyladenine,

N1-methylcytosine, N3-methylcytosine) and their unmethylated counterparts, or nucleoside N7-methylguanosine. Only methylated, positively charged bases are bound. Key features that characterize the enhanced stacking interaction with two aromatic side chains and play a dominant role in cap recognition are described.
22 June 1999, *Proceedings of the National Academy of Science USA*

☐ Structure of human pro-matrix metalloproteinase-2: activation mechanism revealed. Morgunova E, Tuuttila A, Bergmann U, Isupov M, Lindquist Y, Schneider G and Tryggvason K (1999). *Science* 284, 1667-1670.
Matrix metalloproteinases (MMPs) catalyse extracellular matrix degradation. Control of their activity is a promising target for therapy of diseases characterized by abnormal connective tissue turnover. MMPs are expressed as latent proenzymes that are activated by proteolytic cleavage that triggers a conformational change in the propeptide (cysteine switch). The structure of proMMP-2 reveals how the propeptide shields the catalytic cleft and that the cysteine switch may operate through cleavage of loops essential for propeptide stability.
4 June 1999, *Science*

☐ Crystal structure of the human papillomavirus type 18 E2 activation domain. Harris SF and Botchan MR (1999). *Science* 284, 1673-1677.
The papillomavirus E2 protein regulates viral transcription and DNA replication through interactions with cellular and viral proteins. The amino-terminal activation domain, which represents a protein class whose structural themes are poorly understood, contains key residues that mediate these functional contacts. The crystal structure of a protease-resistant core of the human papillomavirus type 18 E2 activation domain reveals a novel fold creating a cashew-shaped form with a glutamine-rich α helix packed against a β-sheet framework. The protein surface shows extensive overlap of determinants for replication and transcription.
4 June 1999, *Science*

☐ Crystal structure of the Zα domain of the human editing enzyme ADAR1 bound to left-handed Z-DNA. Schwartz T, Rould MA, Lowenhaupt K, Herbert A and Rich A (1999). *Science* 284, 1841-1845.
The editing enzyme double-stranded RNA adenosine deaminase includes a DNA binding domain, Zα, which is specific for left-handed Z-DNA. The 2.1 Å crystal structure of Zα complexed to DNA reveals that the substrate is in the left-handed Z conformation. The contracts between Zα and Z-DNA are made primarily with the 'zigzag' sugar-phosphate backbone, which provides a basis for the specificity for the Z conformation. A single base contact is observed to guanine in the *syn* conformation, characteristic of Z-DNA. Intriguingly, the helix-turn-helix motif, frequently used to recognise B-DNA, is used by Zα to contact Z-DNA.
11 June 1999, *Science*

☐ Structure of the ***Escherichia coli*** fumarate reductase respiratory complex. Iverson TM, Luna-Chavez, Cecchini G and Rees DC (1999). *Science* 284, 1961-1966.
The integral membrane protein fumerate reductase catalyses the final step of anaerobic respiration when fumarate is the terminal electron acceptor. Fumarate reductase consists of four subunits that contain a covalently linked flavin adenine dinucleotide, three different iron-sulfur clusters, and at least two quinones. The crystal structure of intact fumarate reductase has been solved at 3.3 Å resolution and demonstrates that the cofactors are arranged in a nearly linear manner from the membrane-bound quinone to the active site flavin. Although fumarate reductase is not associated with any proton-pumping function, the two quinones are positioned on opposite sides of the membrane in an arrangement similar to that of the organisation observed for cytochrome bc1.
18 June 1999, *Science*

☐ Crystal structure of the Atx1 metallochaperone protein at 1.02 Å resolution. Rosenzweig AC, Huffman DL, Hou MY, Wernimont AK, Pufahl RA and O'Halloran TV (1999). *Structure* 7, 605-617.
The Atx1 structure represents the first structure of a metallochaperone protein, and is one of the largest unknown structures solved by direct methods. The structural features of the metal-binding site support the proposed Atx1 mechanism in which facile metal ion transfer occurs between metal-binding sites of the diffusible copper-donor and membrane-tethered copper-acceptor proteins. The Atx1 structural motif represents a prototypical metal ion trafficking unit that is likely to be employed in a variety of organisms for different metal ions.
25 May 1999, *Structure*

☐ Filamentous phage infection: crystal structure of g3p in complex with its coreceptor, the C-terminal domain of TolA. Lubkowski J, Hennecke F, Plückthun A and Wlodawer A (1999). *Structure* 7, 711-722.
Infection of male *Escherichia coli* cells by filamentous Ff bacteriophages involves interaction of the phage minor coat gene 3 protein (g3p) with the integral membrane protein TolA. G3p consists of three domains (N1, N2, and CT). The crystal structure of the complex between g3p N1 and TolA D3 was obtained by fusing these domains with a long flexible linker. Despite the lack of topological similarity between TolA D3 and g3p N2, both domains interact with the same region of the g3p N1 domain. The fold of TolA D3 is not similar to any previously known protein motifs.
1 June 1999, *Structure*

☐ Crystal structure of two CD46 domains reveals an extended measles virus-binding surface. Casasnovas JM, Larvie M and Stehle T (1999). *EMBO J.* 18, 2911-2922.
The cell surface receptor for measles virus in humans is CD46, a complement cofactor. The crystal structure of the measles virus-binding fragment of CD46 reveals two glycosylated short

consensus repeats with a pronounced interdomain bend and some flexibility at the domain interface. Amino acids involved in measles virus binding define a large, glycan-free surface that extends from the top of the first to the bottom of the second repeat. The extended virus-binding surface of CD46 differs strikingly from those reported for the human virus receptor proteins CD4 and intercellular cell adhesion molecule-1 (ICAM-1), suggesting that the CD46 structure utilizes a novel mode of virus recognition.
1 June 1999, *The EMBO Journal*

☐ Functional glycan-free adhesion domain of human cell surface receptor CD58: design, production and NMR studies. Sun Z, Dötsch V, Kim M, Li J, Reinherz EL and Wagner G (1999). *EMBO J.* 18, 2941-2949.

A general strategy is presented here for producing glycan-free forms of glycoproteins without loss of function by employing apolar-to-polar mutations of surface residues in functionally irrelevant epitopes. The success of this structure-based approach was demonstrated through the expression in *Escherichia coli* of a soluble 11 kDa adhesion domain extracted from the heavily glycosylated 55 kDa human CD58 ectodomain. The solution structure was subsequently determined and binding to its counter-receptor CD2 studied by NMR. The new structural information supports a 'hand-shake' model of CD2-CD58 interaction.
1 June 1999, *The EMBO Journal*